

The University of Chicago

ATTEMPTED AUTOTRANSPLANTATION OF THE ADRENAL CORTEX

A PART OF THE DISSERTATION SUBMITTED
TO THE GRADUATE FACULTY IN CANDIDACY
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF PHYSIOLOGY

By
ADELAIDE JOHNSON

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ATTEMPTED AUTOTRANSPLANTATION OF THE ADRENAL CORTEX

ADELAIDE JOHNSON

From the Physiological Laboratories of the University of Chicago

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Transplantation of tissues has been attempted with varying degrees of success for a long time, in a variety of species. Clinically, skin and bone have been successfully transplanted and experimentally a number of tissues, such as thyroid and parathyroid (Manley and Marine, 1916), stomach (Ivy and Farrell, 1925), and pancreas (Ivy and Farrell, 1926) have been autotransplanted. Homotransplants are more rare, although such grafts have been reported for the parathyroids (Erdheim quoted by Dragstedt, 1927) and hypophysis (Allen, 1921). It is doubtful whether functioning heterotransplants have ever been made.

Attempts to transplant the adrenal cortex have been made repeatedly, but on the whole the few "takes" reported are open to criticism. Stilling (1905) reported success on histological evidence alone, as did Busch et al. (1905) (1908), who in addition did cite two instances where the physiological criteria of success were fulfilled. On a statistical basis Sundberg (1925) reported "takes" in rabbits, about twenty per cent of which, however, have accessory cortical tissue adequate to support life. True transplants by the pedicle method, so successful in both the human skin and also the gastric mucosa (Ivy and Farrell, 1925) and pancreas (Ivy and Farrell, 1926), have failed in the hands of Haberer and Stoerk (1918) and Oldberg (1929). Zwemer (1927) and others have also been unable to produce growing transplants.

METHOD. The dog was chosen as the experimental animal because accessory adrenal glands are very rare (Stewart and Rogoff, 1928). This criterion of success was adopted: the transplant must maintain the animal alive and well after removal of both glands; the animals must die with the characteristic symptoms when the graft is removed; there must be histological evidence of cortical tissue in the transplants; there must be no accessory cortical tissue found on careful search at autopsy.

Transplants were attempted to the thyroid, because of its vascularity, and the omentum, testis and kidney, because of previous suggestions of success in these tissues. In one series emulsions of cortical tissue were injected into the splenic vein, the aim being to make multiple small trans-

plants to the liver, such as occurs presumably in carcinoma metastases. Furthermore, Manley and Marine (1916) have made autografts of the thyroid into blood vessels, using the jugular vein.

At operation under morphine-ether anesthesia the host tissue was exposed before doing the adrenalectomy. For this latter a three to four inch incision was made in the abdominal wall about an inch lateral to the border of the rectus abdominis muscle and the gland approached from its ventral surface. The right gland was dissected away with an orangewood stick, care being exercised not to injure the splanchnic nerve. When the gland was freed except for the craniad portion, where the artery enters, the lumbo-adrenal vein was ligated proximal and distal to the gland, and the excision completed as rapidly as possible. The adrenal artery rarely required ligation. Tamponade for a minute or two was usually sufficient whenever the artery bled.

While one operator prepared thin slices of cortex from the excised gland the other incised the host organ. Sometimes before implantation the pieces of cortex were placed in warm Ringer's solution through which oxygen was bubbled for two or three minutes. The slices were inserted in place, usually within about five minutes from the time of occlusion of the gland's vessels, and the host tissue sutured. The sutures never passed through the transplant. Lastly, the abdominal wound was closed.

After experimenting with recovery periods varying from one to eight weeks, four weeks was selected as the optimum. At the second operation the left gland was excised as rapidly and with as little trauma as possible, using essentially the above described technique. The time elapsing between making the incision and finishing suturing was about twenty minutes. In some instances the transplantation was done at the second operation, and sometimes at both operations.

The animals, which had previously been on a diet of meat, bread, bone meal, and water, were now given milk, sugar, bread, bone meal and water, and were kept in a warm room until death. Autopsy was always done and the site of the transplant examined carefully. In approximately the first half of the dogs run, death often occurred within three days. Surgical trauma was undoubtedly a factor in these early deaths, which presumably would have occurred even if there was present a growing transplant producing the minimum physiological action necessary for life. Histological studies of the site of the transplantation were therefore made in these. If the microscopic evidence were positive, little could be concluded. But if it were negative, it would be safe to assume that death would have occurred in a few days even had there been no surgical trauma. Later in the work, when animals lived four to six days and death could be attributed to adrenal insufficiency, histological studies were not made.

Nodules suspected of being accessory cortical tissue were also examined

microscopically, but no rests were found in over 150 dogs of this and other series. The viscera of the chest and abdomen were examined routinely, grossly and sometimes microscopically. Throughout the experiment control animals were operated and treated as described above, except that no transplantation was done.

RESULTS. In most cases complete absorption of the transplant with scar tissue formation was seen. In a few instances there were microscopic suggestions of cortical tissue, but vascularization was never observed. These few anatomical "takes" were entirely inadequate to support life, either because they were too small or else because they were not physiologically active. By physiological criteria the transplants never took. Table 1 gives a summary of the results. It will be seen that the average survival time for animals with transplants was slightly under that of the controls.

TABLE 1

Average time of survival of transplanted and control dogs following second adrenalectomy

SITE OF TRANSPLANT	ALL DOGS OF SERIES		ONLY DOGS SURVIVING AT LEAST 3 DAYS		LONGEST SURVIVAL TIME
	Number of dogs	Days survival	Number of dogs	Days survival	
					<i>days</i>
Thyroid.....	19	3	8	4.5	6
Thyroid and omentum.....	3	2.5	1	3	3
Kidney.....	11	2.5	3	5	10
Emulsions to liver.....	5	5	5	5	7
Testis.....	8	4.5	6	5.5	7
All transplants.....	46	3.4	23	5	10
Controls.....	14	4	6	5	8

The third and fourth columns of the table give the results only on those dogs which survived at least three days post-operatively. These dogs may be considered to have died from adrenal insufficiency, and not from surgical trauma. However, the entire series of sixty dogs is of value, although 31 of them died in one to three days, for in these the histological evidence for failure is adequate. Because averages may sometimes be deceptive there is also given the longest survival time in each series.

Incidentally, we confirm the findings of Stewart and Rogoff (1926) and others regarding the behavior of dogs after double adrenalectomy: post-operative depression, recovery from this with resumption of eating and other normal activities, and then a rather sudden decline with refusal of food, vomiting of bile tinged fluid, bloody diarrhea, asthenia, "hallucinations," and death from respiratory failure. Pathological findings were also essentially those of previous workers: hemorrhagic infiltration of the gas-

tro-intestinal mucosa and pancreas, blood in the intestinal lumen, and gastric ulcers.

CONCLUSIONS

Using the methods described we were uniformly unsuccessful in attempts to autotransplant the adrenal cortex of 46 dogs to the thyroid, omentum, testis, kidney and liver.

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